Double Edge: CDK2AP1 in Cell-cycle Regulation and Epigenetic Regulation.

Journal: J Dent Res

Publication Year: 2011

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PubMed link: 21865592

Funding Grants: Novel Mechanism in Self-Renewal/Differentiation of Human Embryonic Stem Cells

Public Summary:
In this review, we have examined several lines of evidence demonstrating the significance of cell-cycle regulatory mechanisms in cancer development as well as in stem cell maintenance and differentiation. It is generally considered that cancer cells are quite different from stem cells, since they are generated from fully differentiated cells. However, two important cellular and molecular similarities between cancer cells and stem cells provide scientific justification for how studying stem cell models can be beneficial in understanding cancer biology. First, cancer cells share many molecular pathways that are important in the maintenance and differentiation of stem cells. Second, evidence supports that genesis of cancer cells may involve a de-differentiation process, which eventually causes terminally differentiated cellular phenotypes to revert to a stem-cell-like state. This involves reactivation or inactivation of key molecular and cellular pathways that resemble those in stem cells. In addition, the emerging concept of cancer stem cells provides us with sufficient justification to use stem cells as a proper experimental model to understand the mechanism of the genesis and development of cancers. As reviewed in this article, CDK2AP1 is involved in both cancer development and stem cell fate. Moreover, CDK2AP1 is emerging as one of the key molecules involved in the interplay between cell-cycle regulation and epigenetic regulation. CDK2AP1 may potentially be regulating molecular networks, rendering mutual intra-regulatory influences. It is intriguing that a given cell-cycle regulator, such as CDK2AP1, has a dual role in cell-cycle and epigenetic control.

Scientific Abstract:
Cancer research has been devoted toward an understanding of the molecular regulation and functional significance of cell-cycle regulators in the pathogenesis and development of cancers. Cyclin-dependent Kinase 2-associated Protein 1 (CDK2AP1) is one such cell-cycle regulator, originally identified as a growth suppressor and a prognostic marker for human oral/head and neck cancers. Functional importance and the molecular mechanism of CDK2AP1-mediated cell-cycle regulation have been documented over the years. Recent progress has shown that CDK2AP1 is a competency factor in embryonic stem cell differentiation. Deletion of CDK2AP1 leads to early embryonic lethality, potentially through altered differentiation capability of embryonic stem cells. More intriguingly, CDK2AP1 exerts its effect on stem cell maintenance/differentiation through epigenetic regulation. Cancer cells and stem cells share common cellular characteristics, most prominently in maintaining high proliferative potential through an unconventional cell-cycle regulatory mechanism. Cross-talk between cellular processes and molecular signaling pathways is frequent in any biological system. Currently, it remains largely elusive how cell-cycle regulation is mechanistically linked to epigenetic control. Understanding the molecular mechanism underlying CDK2AP1-mediated cell-cycle regulation and epigenetic control will set an example for establishing a novel and effective molecular link between these two important regulatory mechanisms.